

WO 99/42481

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PCT/DE99/00554

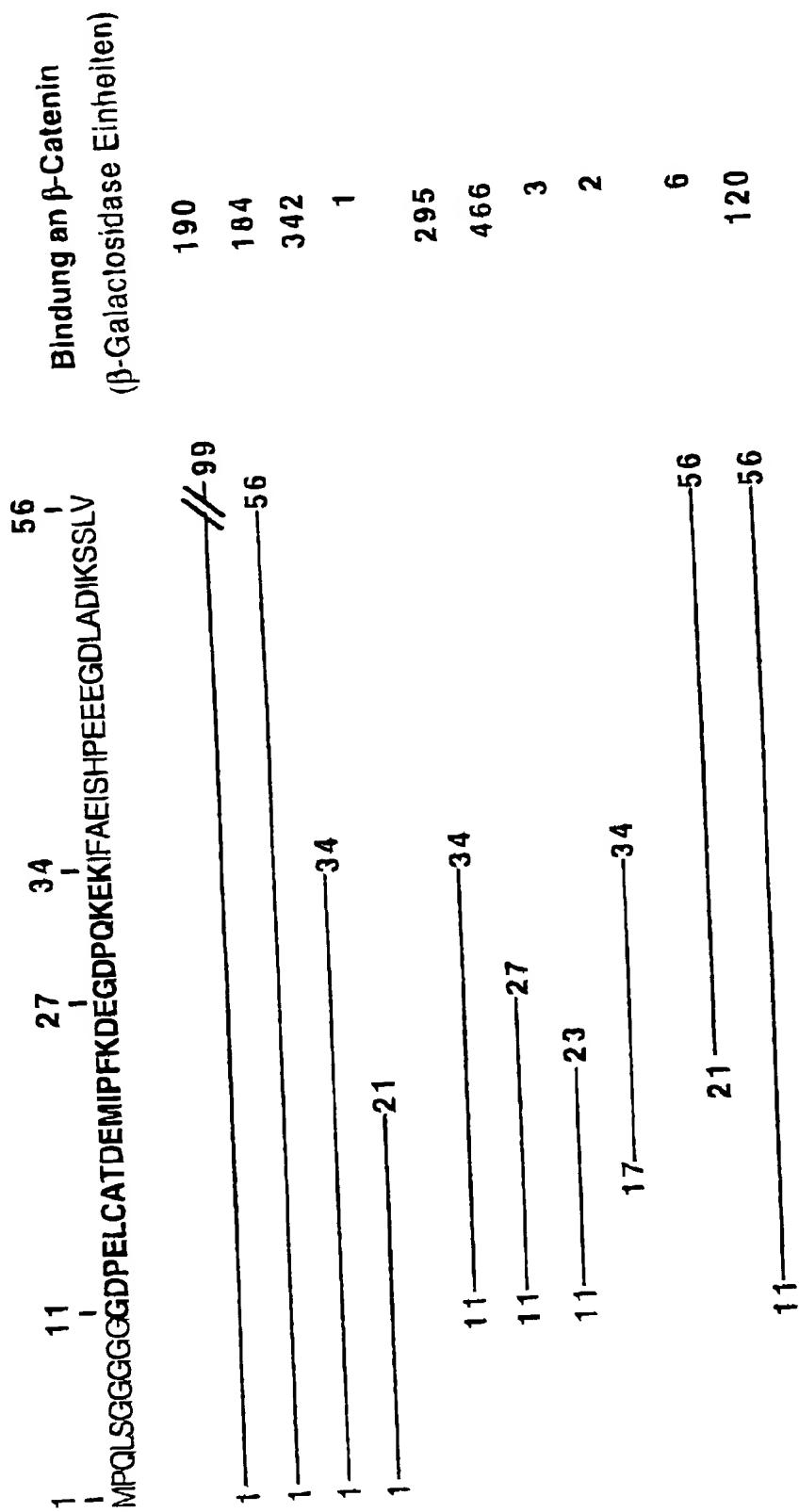
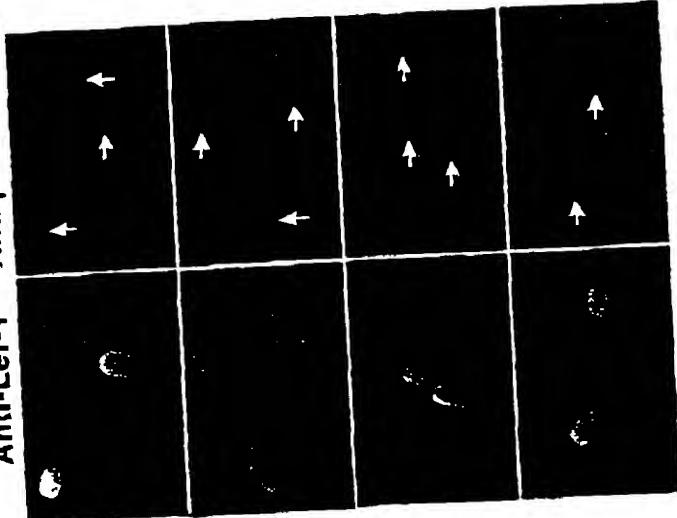
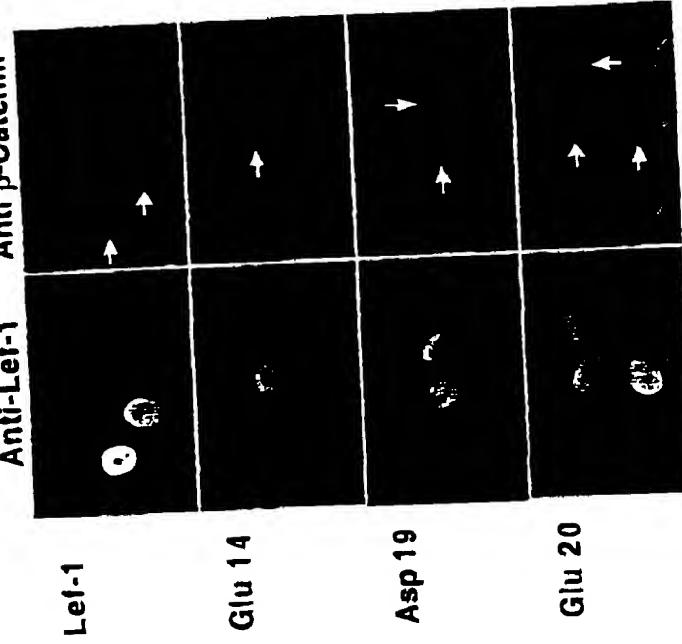


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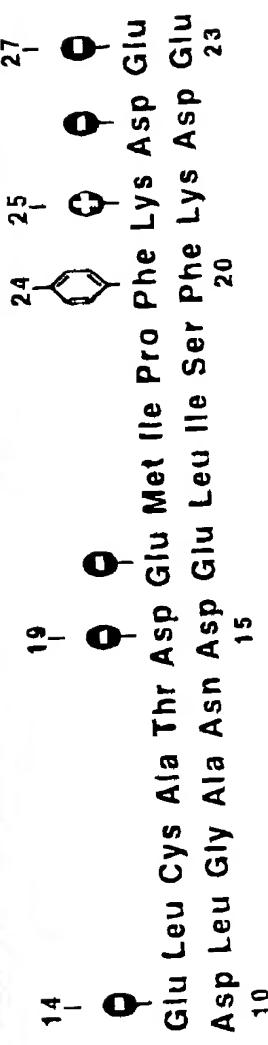
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Anti-Lef-1 Anti  $\beta$ -CateninAnti-Lef-1 Anti  $\beta$ -Catenin

A



B

Abb. 4

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PCT/DE99/00554

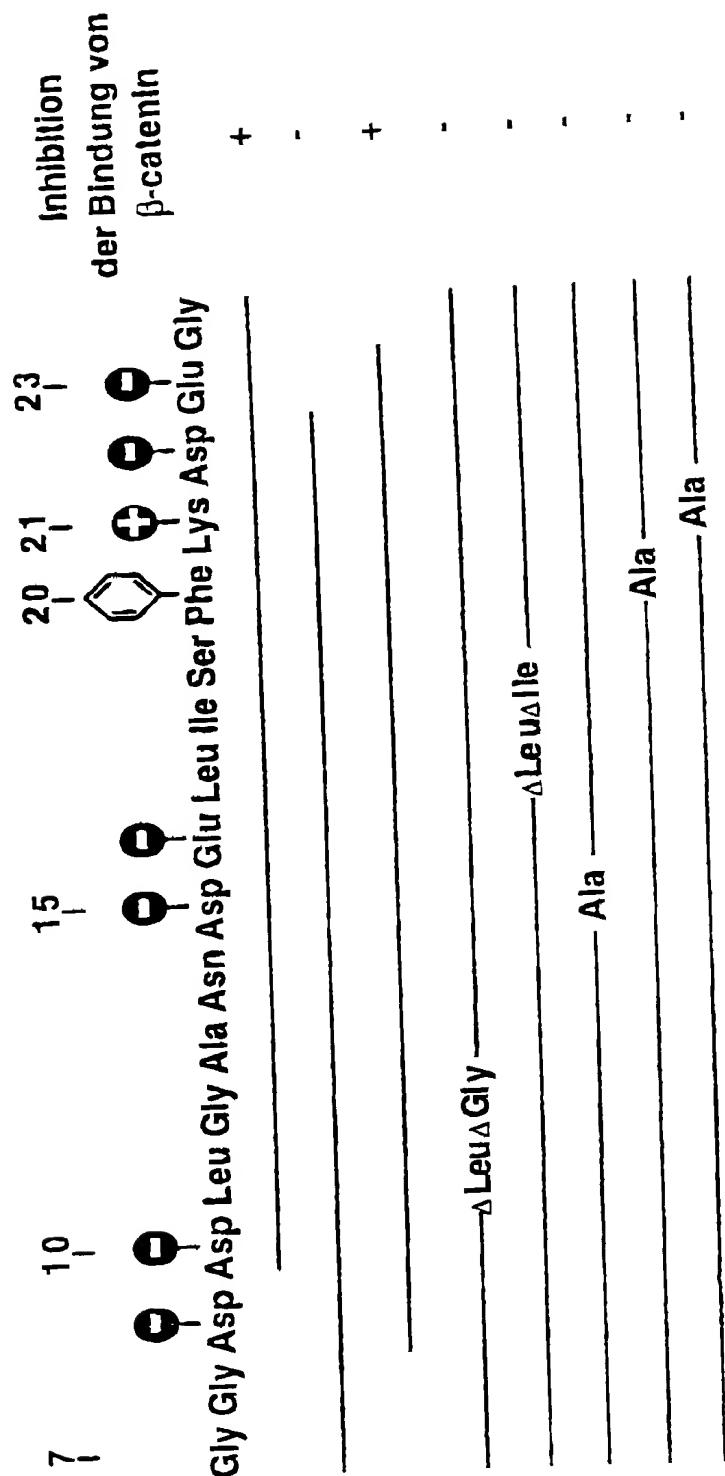


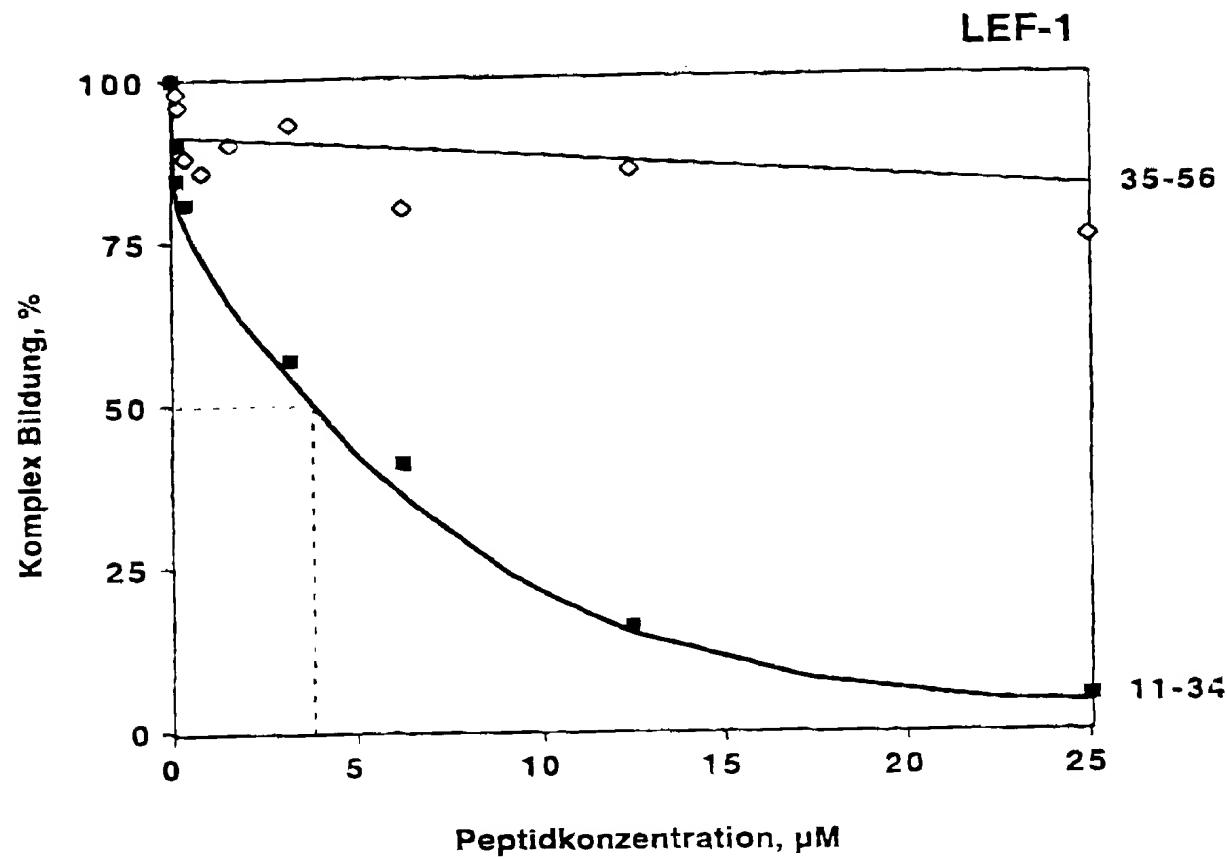
Abb. 2

WO 99/42481

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PCT/DE99/00554

## Inhibition der LEF-1/ $\beta$ -catenin Interaktion durch synthetische Peptide aus der Minimalen Bindungs-Domäne



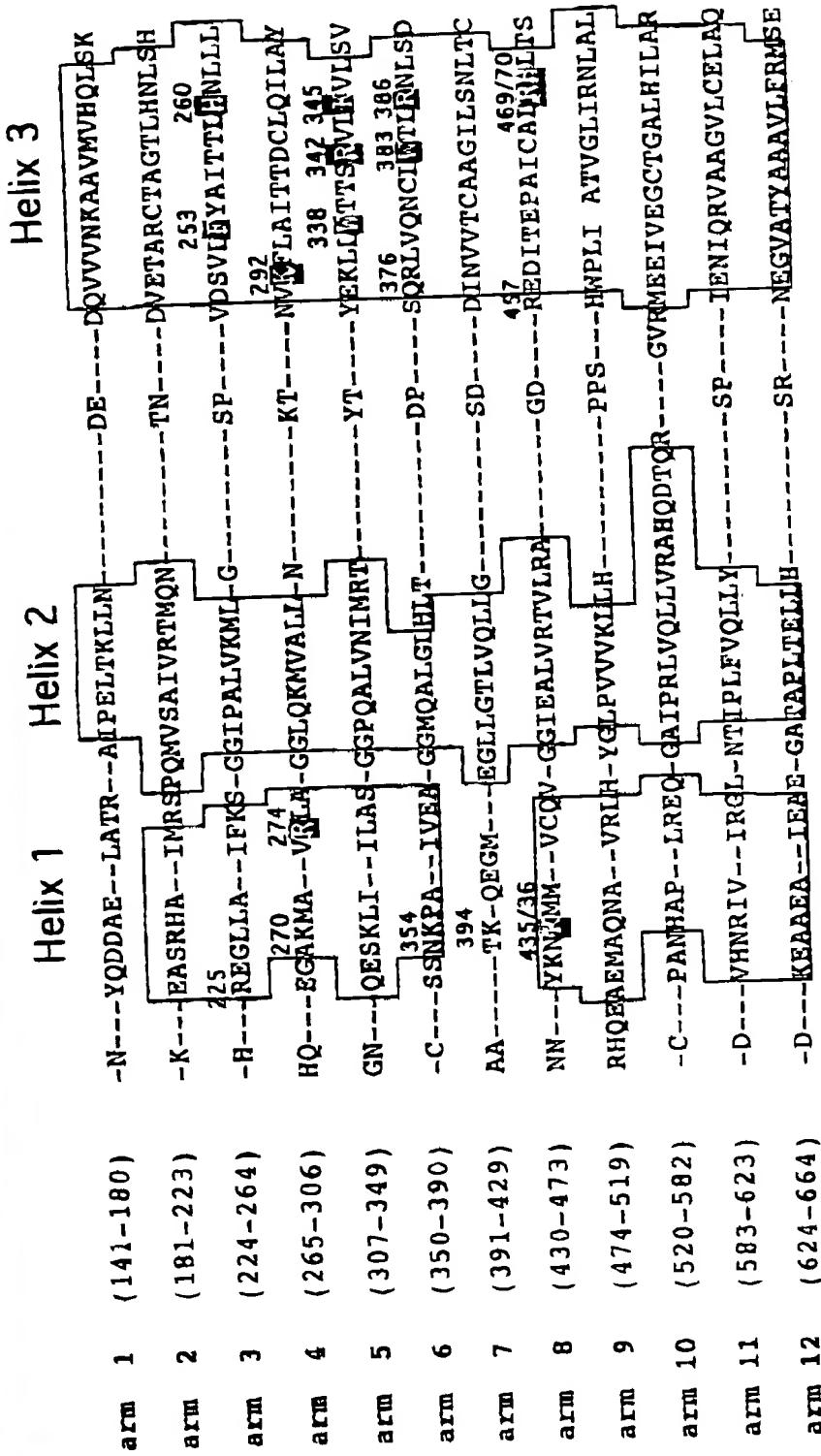
**Abb. 3**

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PCT/DE99/00554

# $\beta$ -Catenin Mutationen mit < 30 % Transaktivierung

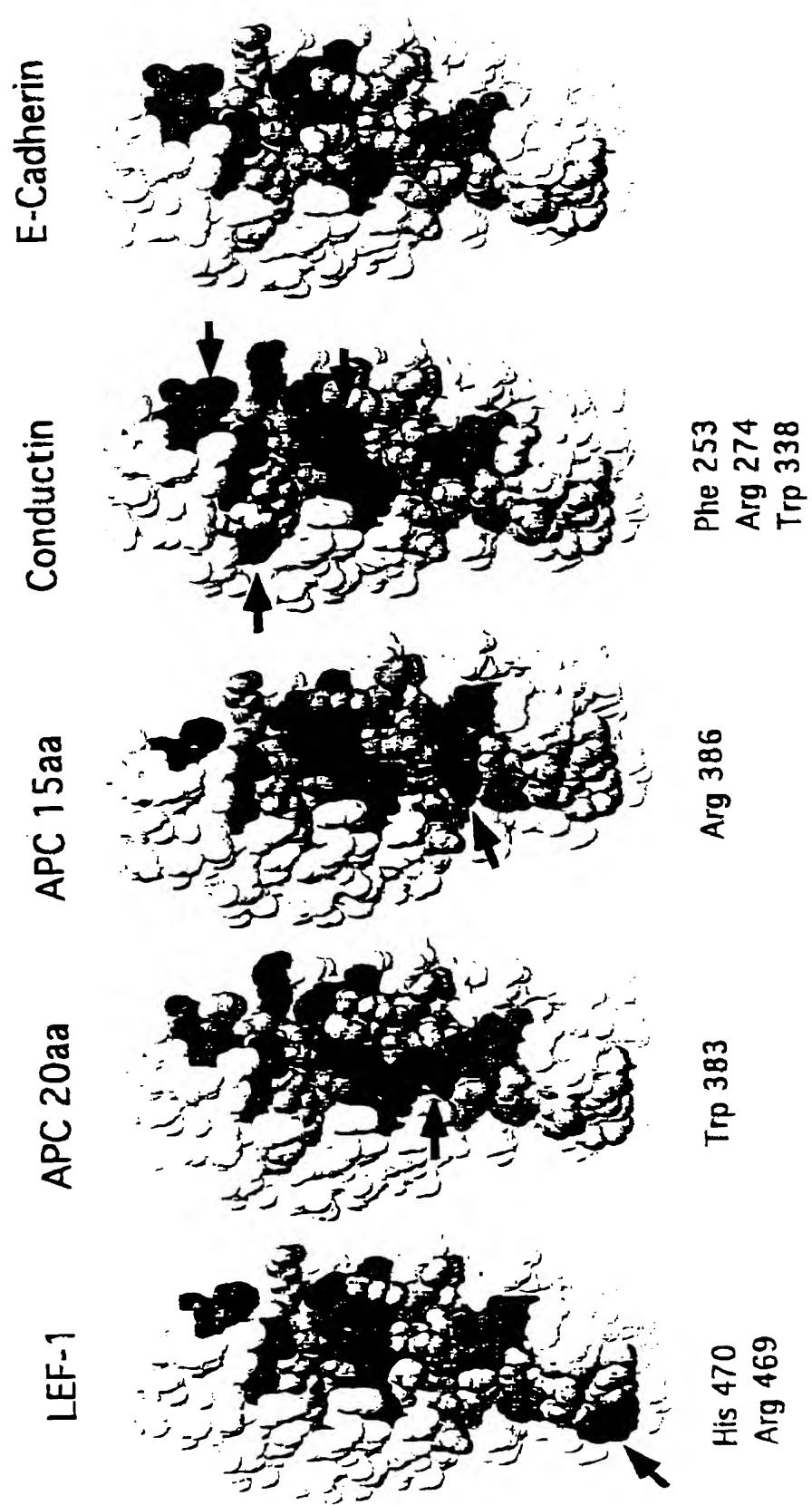


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PCT/DE99/00554

Interaktion von  $\beta$ -Catenin Mutanten mit:



Interaktions-Reporteraktivität:

- 0 - 30 %
- 30- 60 %

→ : Mutation für Interaktionspartner spezifisch

Abb. 6

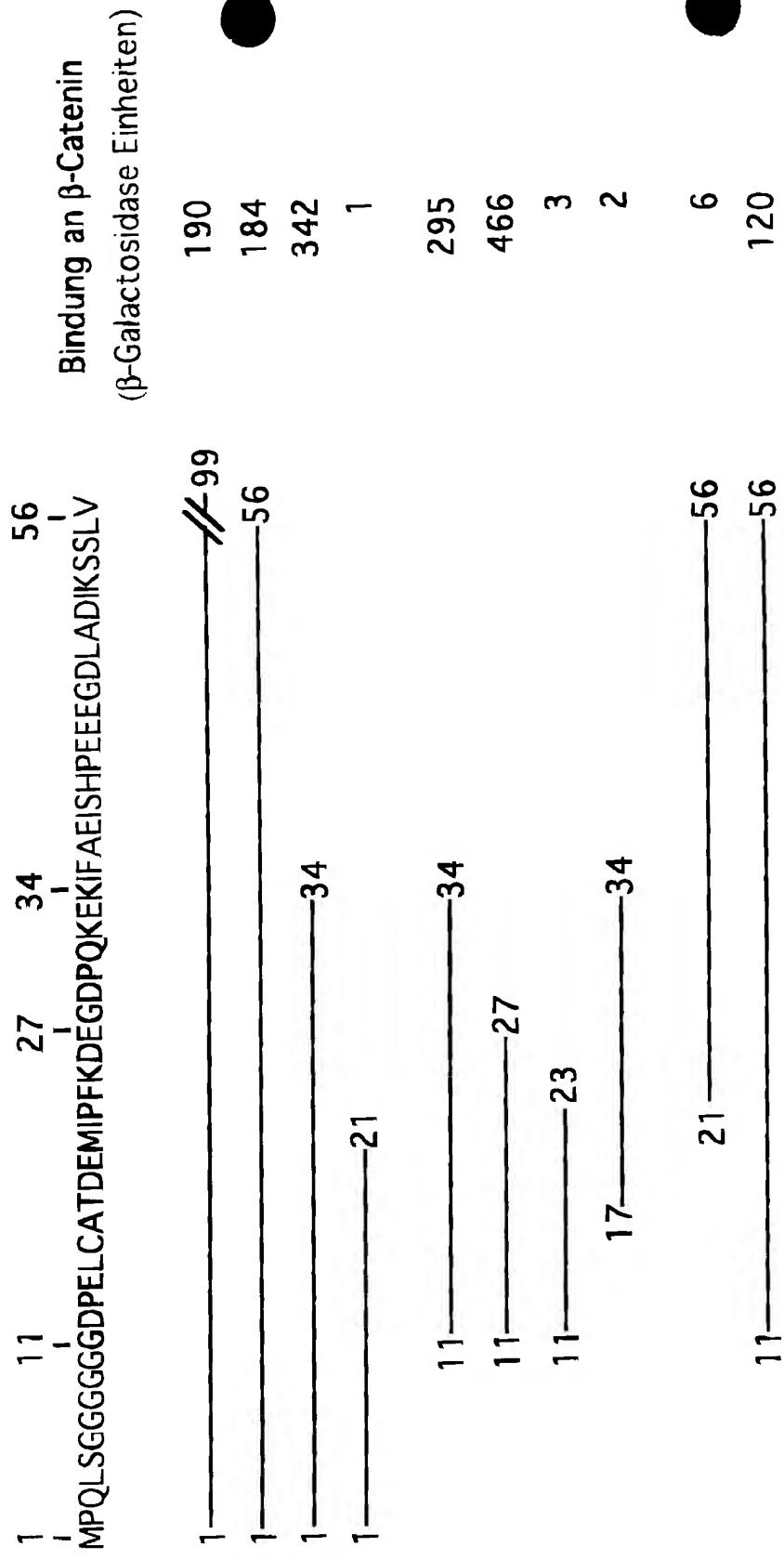


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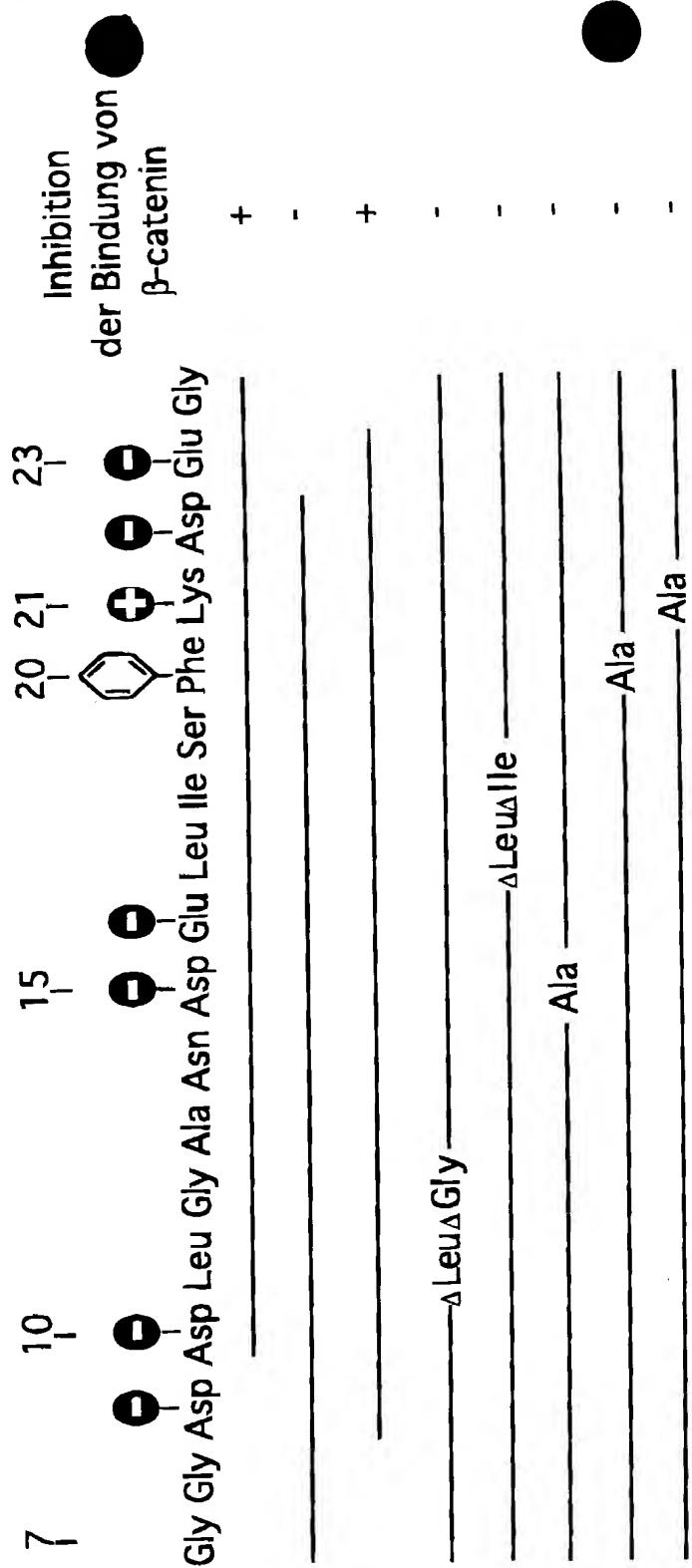


Abb. 2

# Inhibition der LEF-1/ $\beta$ -catenin Interaktion durch synthetische Peptide aus der Minimalen Bindungs-Domäne

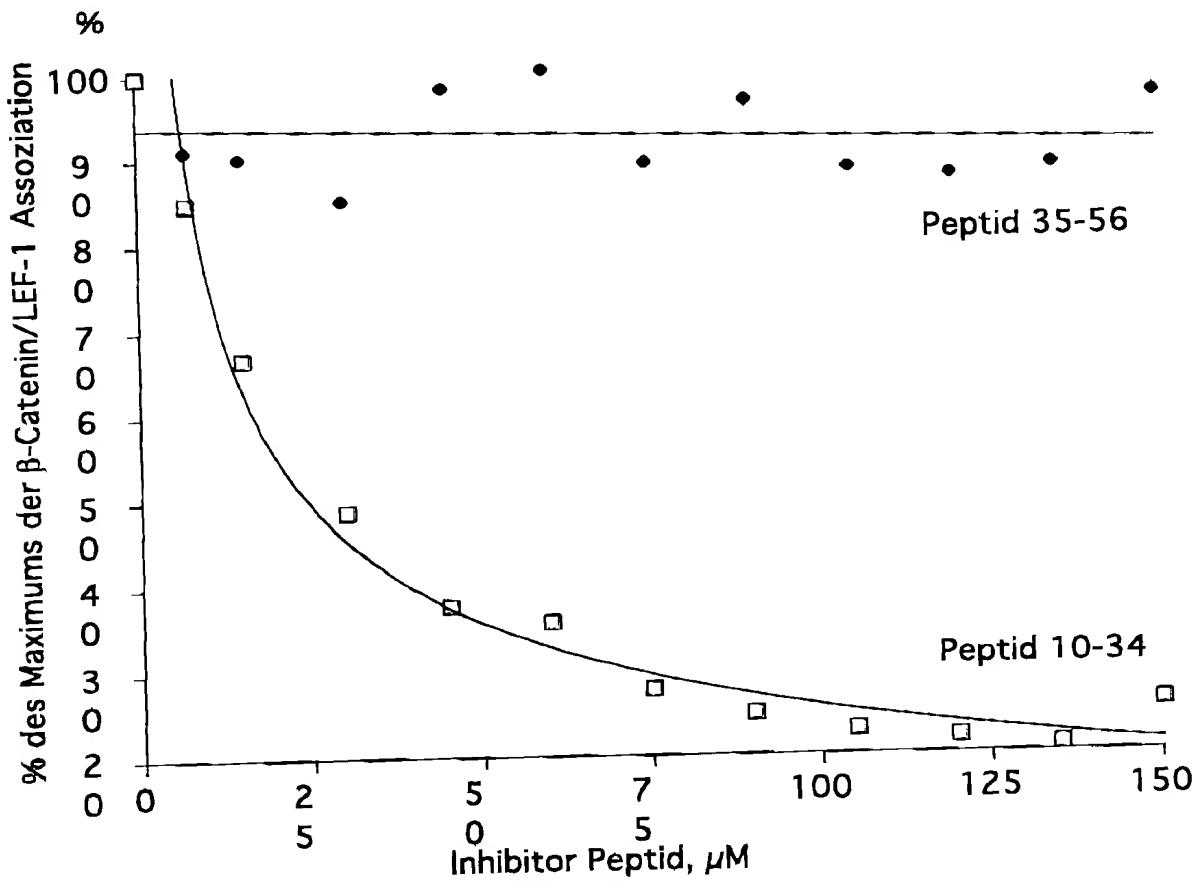


Abb. 3

A                   Anti-Lef-1      Anti  $\beta$ -Catenin

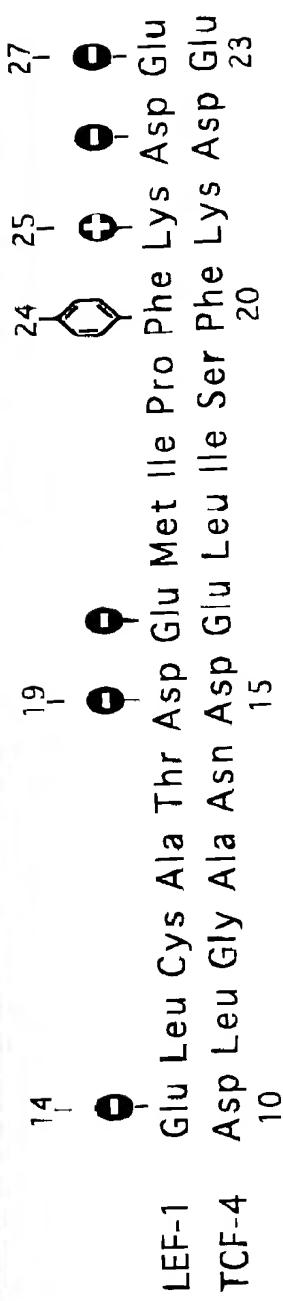
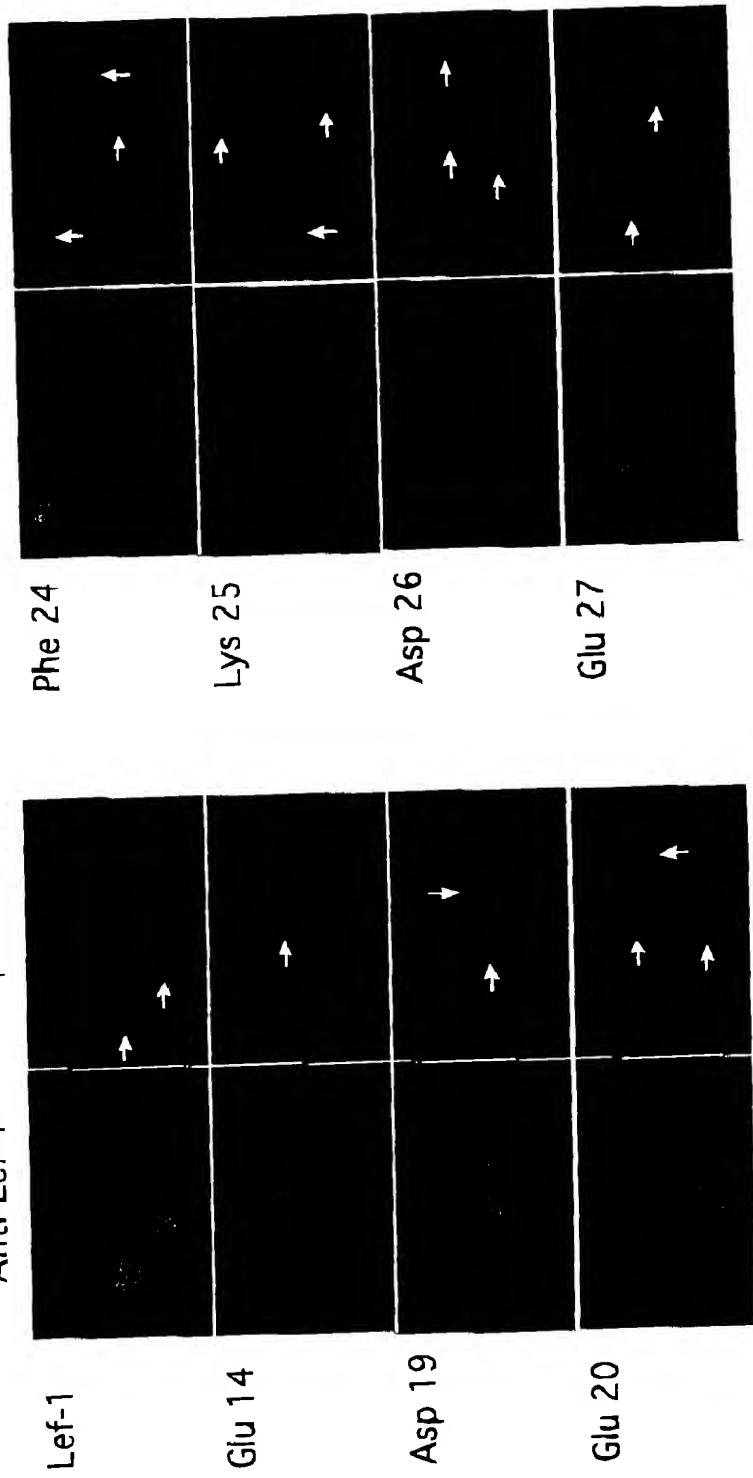
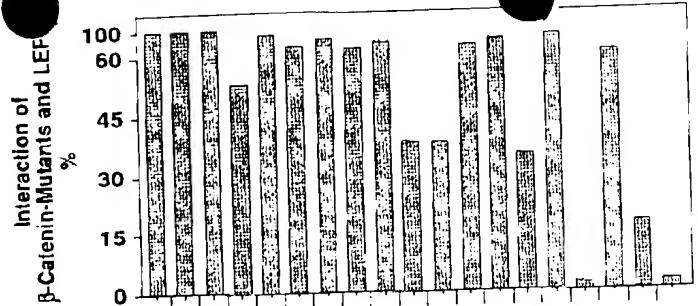
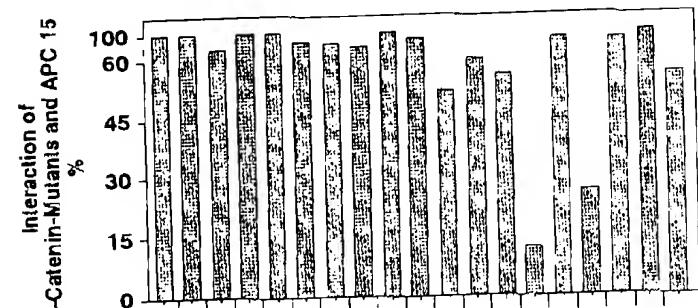
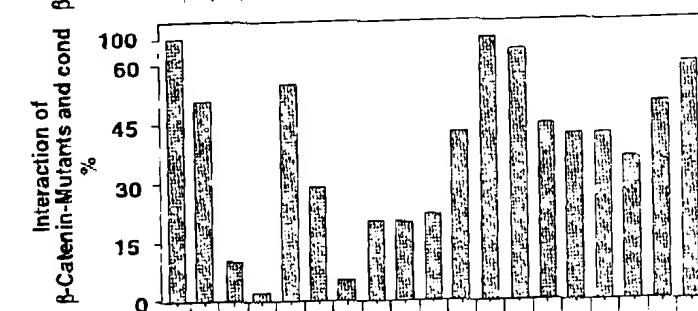
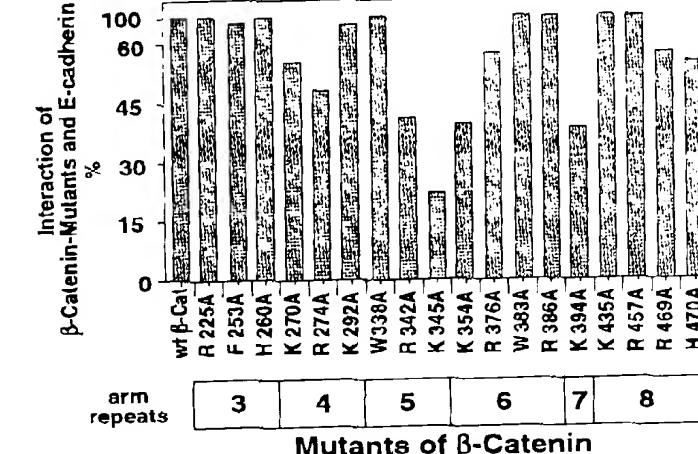


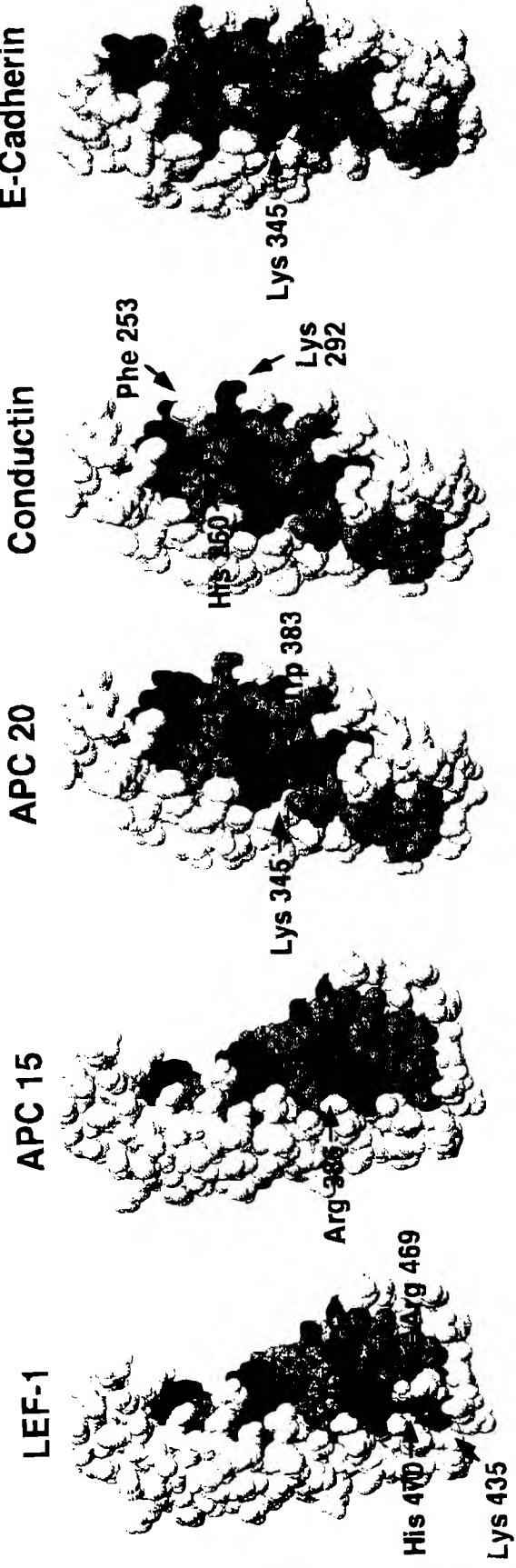
Abb. 4

**a****b****c****d****e**Mutants of  $\beta$ -Catenin

arm repeats      3    4    5    6    7    8

**Abb. 5**

Abb. 6



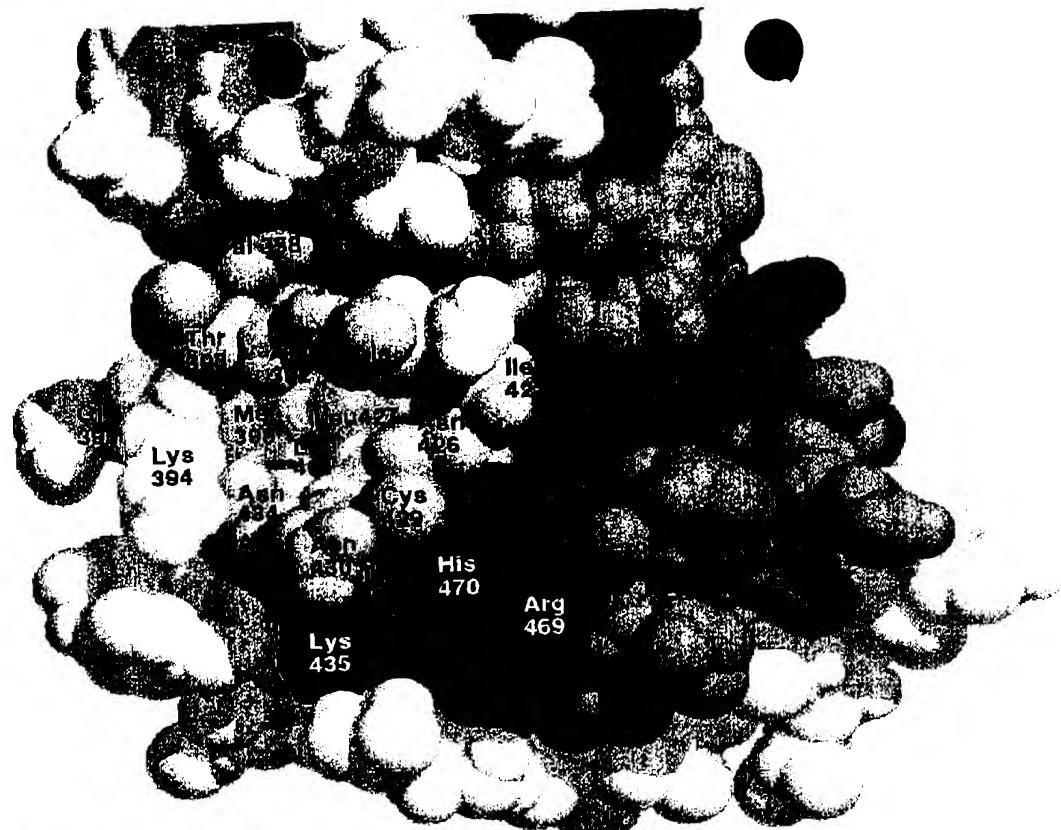
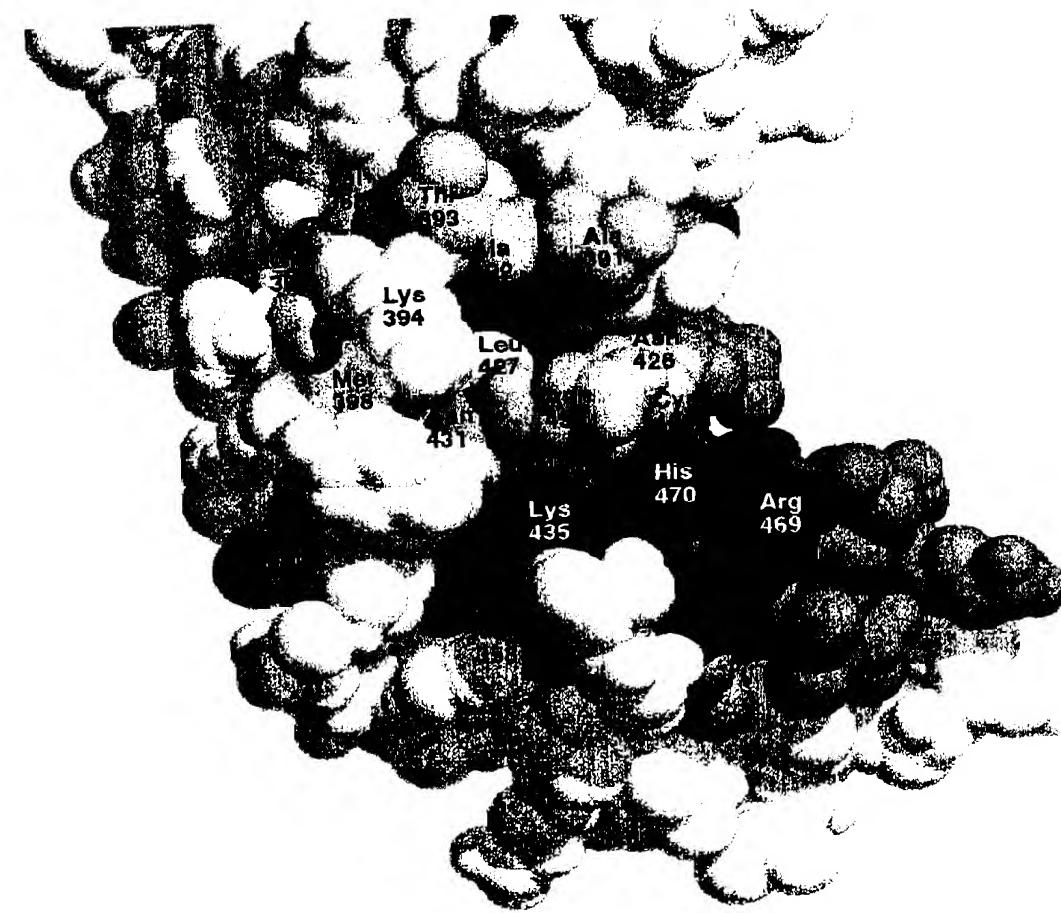
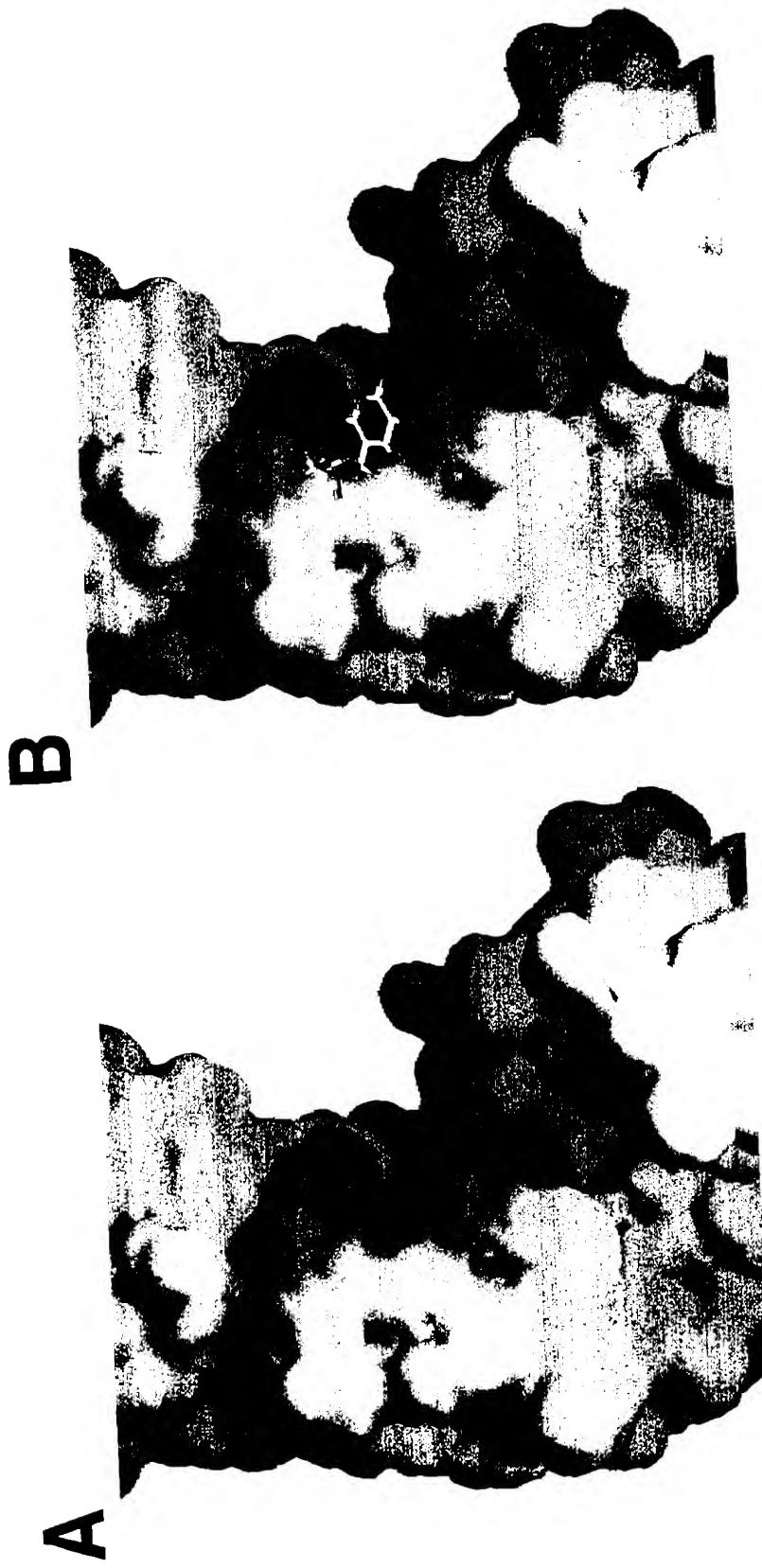
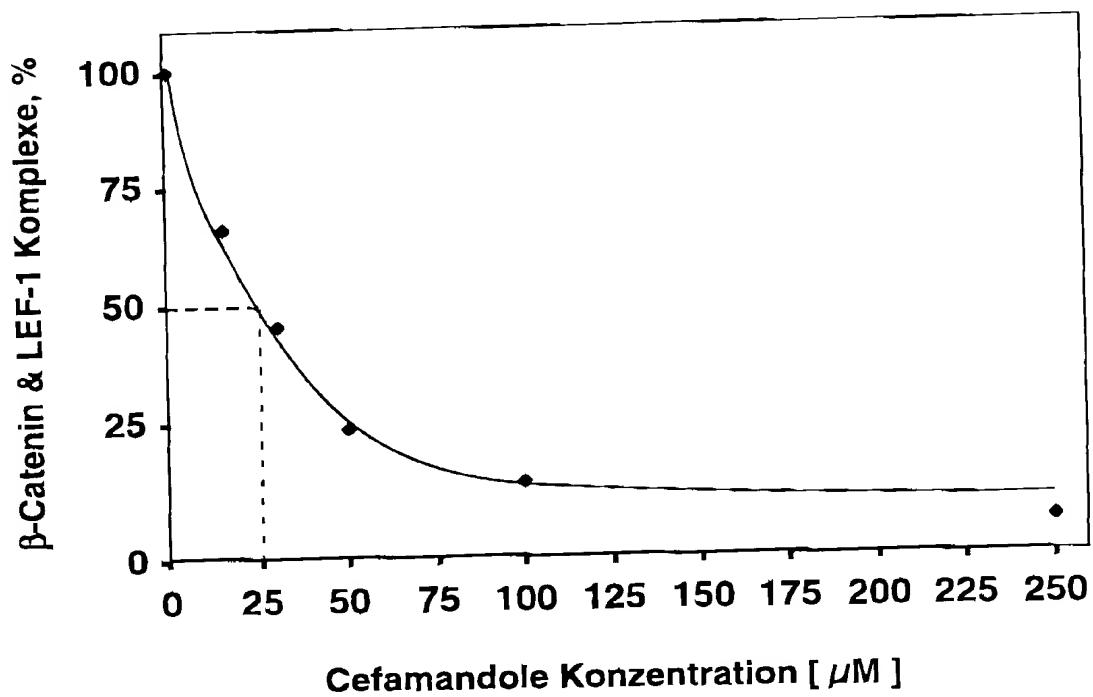
**A****B****Abb. 7**

Abb. 8



**Abb. 9**

## Tab.1

Aminosäuresequenz des humanen  $\beta$ -Catenin (Armadillo-Repeats 3-9)

arm 3	(224 - 264)	<del>HRECLIAFFKSGGFPALVKEAGSPVDSFYLFAITTEANL</del>
arm 4	(265 - 306)	<del>HOEGA MAVRLAGGLQKMVALLNKTNVKFLAITTBCLQILAY</del>
arm 5	(307 - 349)	<del>GNQESKLIIILASGGPQALVNIMRTTYYEKLTWTTSRVLKVLSV</del>
arm 6	(350 - 390)	<del>CSSNKPAIVEAGGMQALGLHLIDPSQRIVQNCLWTIRNLSD</del>
arm 7	(391 - 429)	<del>AATKQEGMEGLLGTIVQLLGSDDDINVVTCAAAGGILSNLTC</del>
arm 8	(430 - 473)	<del>NNYKKNKMMVGEQVGGLIEALVRTVLRAGDREDITEPAICALRHLTS</del>
arm 9	(474 - 519)	<del>RHQJAEERHONAVRHTHYGLPVVVKLIHPPSHPTKATVGLFRNIAL</del>

Tab.2

**Interaktion von  $\beta$ -Catenin Mutanten mit  
LEF-1, APC (20 und 15 Aminosäure -Repeats),  
Conductin und E-Cadherin**

$\beta$ -Catenin Mutanten	arm. Einh.	Interaktion mit				
		LEF-1	APC-20	APC-15	Conductin	E-Cadherin
Phe 253	3	-	40	-	17	-
His 260	3	50	40	100	10	100
Arg 274	4	-	40	-	29	50
Lys 292	4	-	28	-	5	-
Trp 338	5	-	55	-	20	-
Arg 342	5	-	29	-	20	41
Lys 345	5	38	0	-	22	27
Lys 354	6	38	-	54	43	40
Trp 383	6	-	0	59	-	-
Arg 386	6	35		12	45	-
Lys 394	7	-	-	-	42	-
Lys 435	8	-	-	30	42	-
Arg 457	8	-	-	-	36	-
Arg 469	8	17	-	-	-	50
His 470	8	2	47	60	-	-

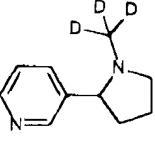
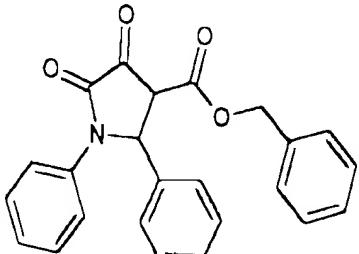
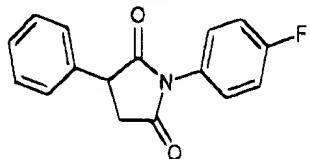
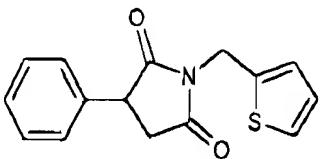
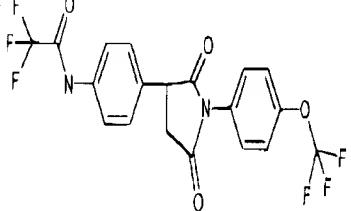
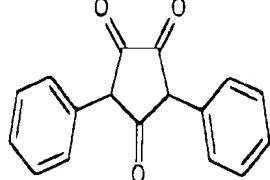
Die Werte geben den prozentualen Anteil der jeweiligen Interaktion im Vergleich zu der mit Wildtyp- $\beta$ -Catenin an. Durch "-" gekennzeichnete Interaktionen entsprechen , 60 -100 % der Wildtyp-Interaktion.

Tab. 3

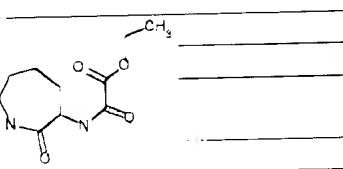
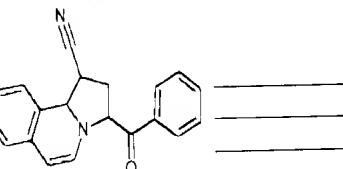
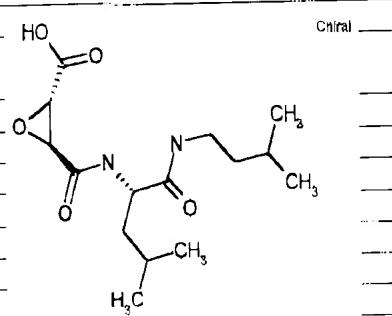
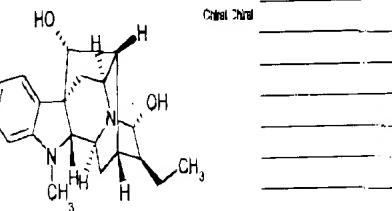
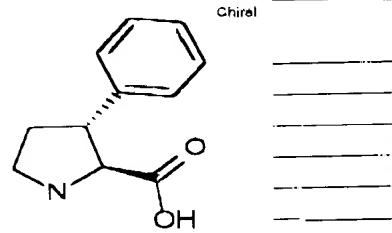
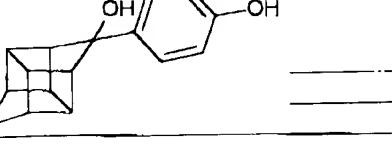
drugs-liste 2000

MOLEKÜLSTRUKTUR	Substanzname	MDL-Nr.
	(-)-ESEROLINE FUMARATE	MFCD00055202
	N-ACETYL-MURAMYL-ALA-ISOGLN-OH	MFCD00065478
	3,6-DIHYDROXYBENZONORBORNANE	MFCD00077441
	N-ACETYL-MURAMYL-ALA-D-ISOGLN-OH	MFCD00077638
	(-)-COTININE	MFCD00077696
	CEFAMANDOLE SODIUM SALT	MFCD00082385

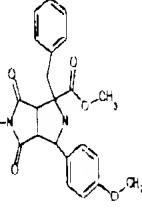
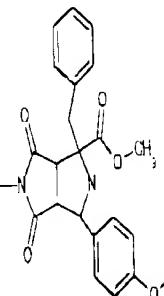
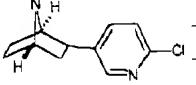
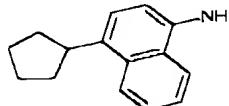
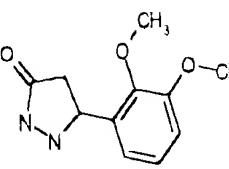
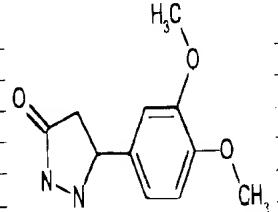
## drugs-liste 2000

	(+/-)-NICOTINE-D3 SALICYLATE SALT	MFCD00083448
	BENZYL 1,2-DIPHENYL-4-HYDROXY-5-OXO-3-PYRROLINE-3-CARBOXYLATE	MFCD00088051
	1-(4-FLUOROPHENYL)-3-PHENYL PYRROLIDINE-2,5-DIONE	MFCD00097831
	3-PHENYL-1-(2-THIENYL METHYL) PYRROLIDINE-2,5-DIONE	MFCD00097832
	N1-(4-[2,5-DIOXO-1-[4-(TRIFLUOROMETHOXY)PHENYL]TETRAHYDRO-1H-PYRROL-3-YL]PHENYL)-2,2,2-TRIFLUOROACETAMIDE	MFCD00100474
	1,3-DIPHENYLCYCLOPENTANE-2,4,5-TRIONE	MFCD00101320

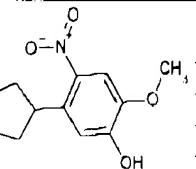
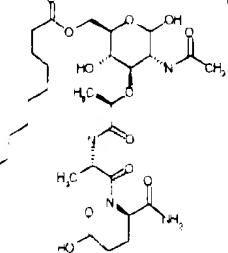
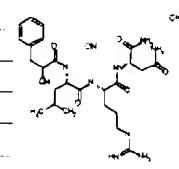
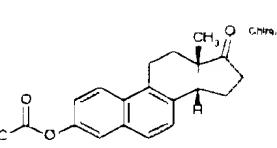
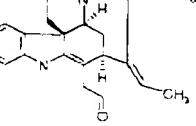
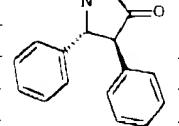
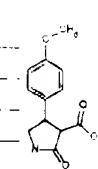
## drugs-liste 2000

	ETHYL 2-OXO-2-[(2-OXOAZEPAN-3-YL)AMINO]ACETATE	MFCD00103142
	3-BENZOYL-1,2,3,10B-TETRAHYDRO-PYRROLO(2,1-A)ISOQUINOLINE-1-CARBONITRILE	MFCD00123443
	L-TRANS-EPOXYSUCCINYL-LEU-3-METHYLBUTYLAMIDE	MFCD00132882
	AJMALINE	MFCD00135652
	(2S,3R)-3-PHENYL PYRROLIDINE-2-CARBOXYLIC ACID	MFCD00142984
	4-(2-HYDROXYOCTAHYDRO-1,3,4-METHENO-2H-CYCLOBUTA(CD)PENTALEN-2-YL)PHENOL	MFCD00155174

## drugs-liste 2000

	METHYL C-4-(4-METHOXYPHENYL)-2-BENZYL-7-PHENYL-6,8-DIOXO-3,7-DIAZABICYCLO[3.3.0]-OCTANE-2-CARBOXYLATE	MFCD00202518
	METHYL C-4-(4-METHOXYPHENYL)-2-BENZYL-7-(4-CHLOROPHENYL)-6,8-DIOXO-3,7-DIAZABICYCLO[3.3.0]-OCTANE-2-CARBOXYLATE	MFCD00202519
	(+/-)-EPIBATIDINE DIHYDROCHLORIDE	MFCD00210196
CIH		
	4-CYCLOPENTYL-NAPHTHALEN-1-YLAMINE, HYDROCHLORIDE	MFCD00227852
CIH		
	5-(2,3-DIMETHOXY-PHENYL)-PYRAZOLIDIN-3-ONE	MFCD00228403
CIH		
	5-(3,4-DIMETHOXY-PHENYL)-PYRAZOLIDIN-3-ONE	MFCD00229211
CIH		

## drugs-liste 2000

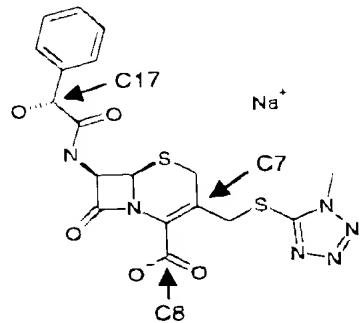
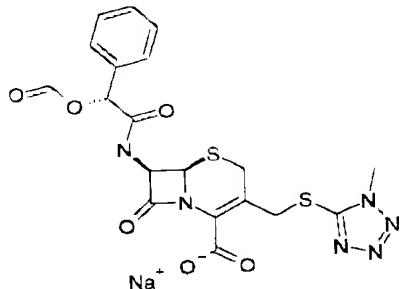
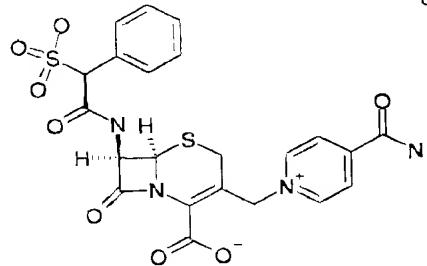
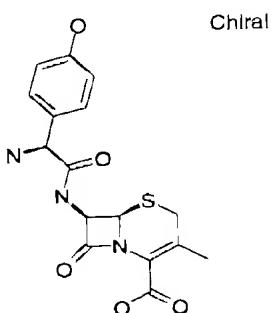
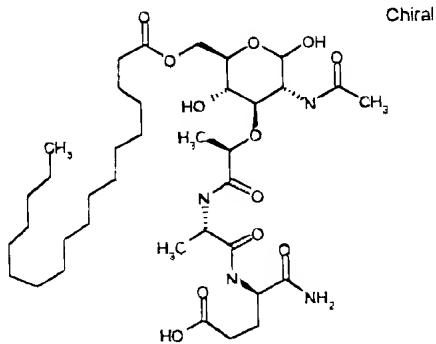
	5-CYCLOPENTYL-2-METHOXY-4-NITRO-PHENOL	MFCD00230901
	AC-(6-O-STEAROYL)-MURAMYL-ALA-D-ISOGlutamine	MFCD00236777
	ANTHO-RNAMIDE	MFCD00236789
	1,3,5(10),6,8(14BETA)-ESTRAPENTAEN-3-OL-17-ONE ACETATE	MFCD00271642
	NORFLUOROCURARINE	MFCD00274483
	4,5-DIPHENYLPYRAZOLIDIN-3-ONE	MFCD00277798
	4-(4-METHOXY-PHENYL)-2-OXO-PYRROLIDINE-3-CARBOXYLIC ACID	MFCD00297824

## drugs-liste 2000

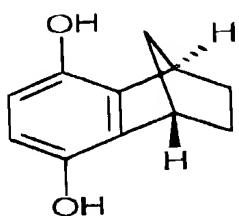
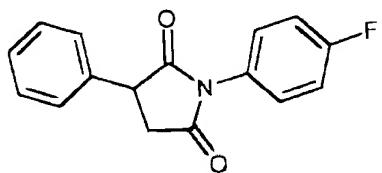
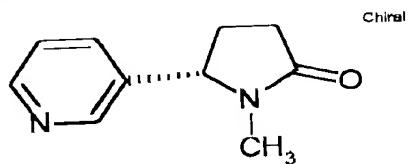
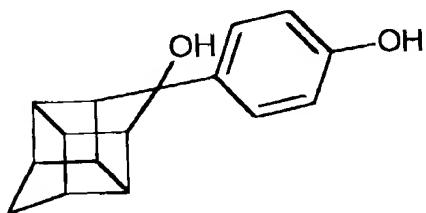
	(+)-EPIBATIDINE HYDROCHLORIDE	MFCD00467208
	FLUOROCURARINE CHLORIDE	MFCD00467712
	(1'S,2'S)-NICOTINE 1'-OXIDE	MFCD00869528
	SPECS SPECS CIF7952	MFCD01114864
	2-ETHYL-2-(3-METHOXYPHENYL)PYRROLIDINE	MFCD01314146
	N-(TERT-BUTYL)-2-(ISOXAZOL-5-YLCARBONYL)DECAHYDROISOQUINOLINE-3-CARBOXAMIDE	MFCD01314517

Tab. 4

Positiv-Liste

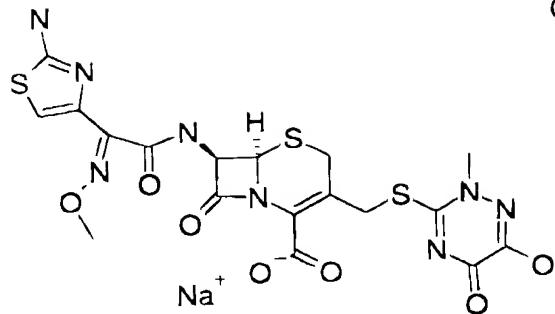
**Molekül-Klasse IA (Inhibitoren vom Cefamandole-Typ)****Cefamandole****Cefamandole-Nafate****Cefsulodin****Cefadroxil****Molekül-Klasse IB****AC-(6-O-STEAROYL)-MURAMYL-ALA-D-ISOGlutamine**

Positiv-Liste

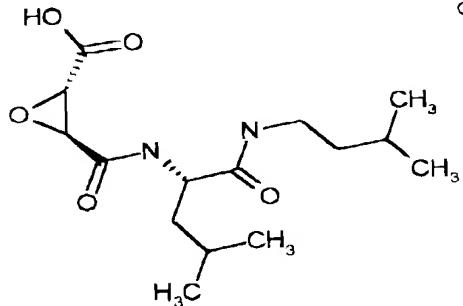
**Molekül-Klasse IC****3,6-DIHYDROXYBENZONORBORNANE****Moleküle mit Modulationswirkung für Molekülklasse I****1-(4-FLUOROPHENYL)-3-PHENYLPYRROLIDINE-2,5-DIONE****(-)-COTININE****4-(2-HYDROXYOCTAHYDRO-1,3,4-METHENO-2H-CYCLOBUTA(CD)PENTALEN-2-YL)PHENOL**

Positiv-Liste

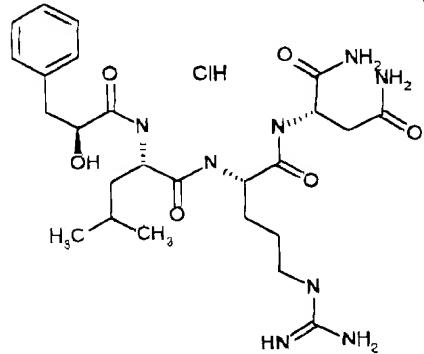
Chiral

**Ceftriaxone**

Chiral

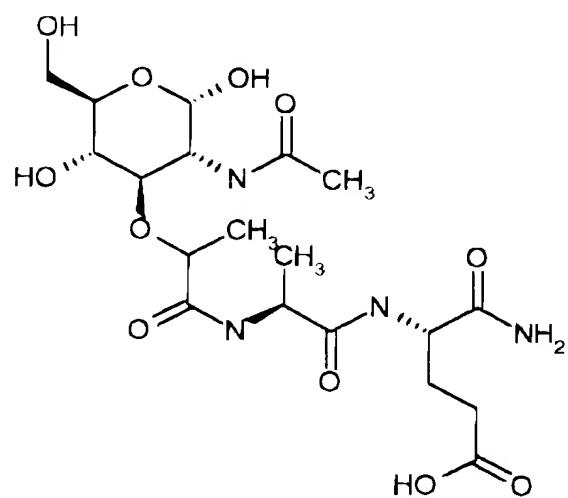
**L-TRANS-EPOXYSUCCINYL-LEU-3-METHYLBUTYLAMIDE**

Chiral

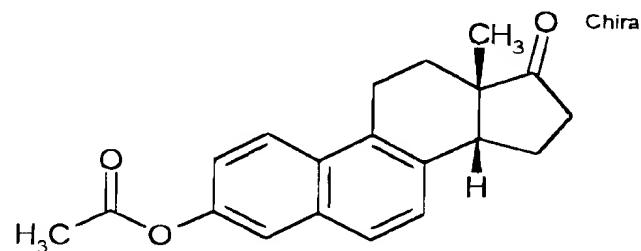
**ANTHO-RNAMIDE**

Positiv-Liste

Chiral

**N-ACETYL-MURAMYL-ALA-ISOGLN-OH**

Chiral

**1,3,5(10),6,8(14BETA)-ESTRAPENTAEN-3-OL-17-ONE ACETATE**